Hiden Analytical Ltd.
420 Europa Boulevard
Warrington WA5 7UN
England

T +44 [0] 1925 445 225
F +44 [0] 1925 416 518
E info@hiden.co.uk
W www.HidenAnalytical.com

Evolved Gas Analysis

A High Sensitivity Study of a Solvent of Recrystallisation in a Pharmaceutical

Authors:
Paul Gabbott and Tim Mann
PETA Solutions
Chalfont Road, Seer Green, Beaconsfield, Buckinghamshire HP9 2FX

Introduction

Thermogravimetric Analysis (TGA) of materials is commonly used to provide information on the weight loss as a sample is heated or held isothermally. Pharmaceutical materials often show weight losses associated with the loss of solvent/ water, desolvation or decomposition of the sample. This information is then used to assess the purity and stability of the material and its suitability for use. The TGA gives a quantitative measure of mass lost from the sample, but it does not provide information on the nature of the products that are lost from the sample, and this information is often required for complete characterisation.

Coupling a mass spectrometer (MS) to a TGA allows evolved gases to be analysed and identified giving this additional valuable information.

Typical applications of TGA-MS include:

- Detection of moisture/solvent loss from a sample. e.g. Loss on Drying or dehydration of a pharmaceutical
- Thermal Stability (degradation) processes
- Study reactions e.g. polymerisations
- Analysis of trace volatiles in a sample e.g. Volatile Organic Content (VOC) testing

Instrumental Setup

In this study a Pyris 1 TGA interfaced to a HPR-20 was used.

Pyris 1 TGA interfaced to the HPR20 QIC

The HPR-20 mass spectrometer is optimised for the analysis of the evolved gases from the TGA and offers the following benefits:

The ability to use either Faraday cup or secondary electron multiplier (SEM) detectors depending on the sensitivity levels required. The SEM offers the ability to detect very low partial pressures of evolved gases below 10^{-8} bar so allowing identification of very low levels of contaminants. The system is able to operate in air so posing no issues for sample changing.

Optional Foreline and Bypass vacuum pumping permits the most efficient pumping of helium which is normally used as a purge gas since it produces no interfering mass ions.

A very flexible heated transfer line allows simple interfacing to the TGA systems. The lightweight heated line can me moved around in use without damage so making the system very robust. Gas transfer uses a wide bore fused silica capillary which gives 16 ml/min flow to the mass spectrometer for highest sensitivity.

An anti-blockage filter has been added to catch high molecular weight material that might block the capillary. This single feature prevents hours of down time and cleaning with no loss of vacuum in the Mass Spectrometer.

Soft Ionisation so the system can be optimised to reduce the splitting of ions leading to a simpler spectrum for analysis.

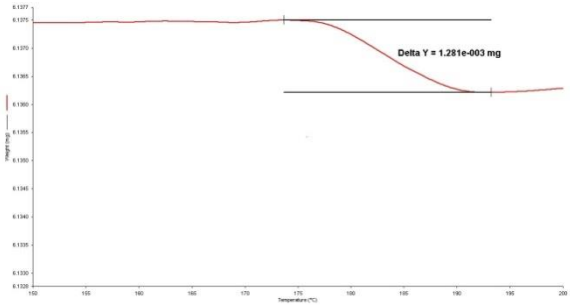
Experiment

In the following study a Pyris 1 TGA interfaced to a HPR-20 was used. The sample was heated to 200°C at 10C/min with Helium gas at 30 ml/min purge. A sample weight of 6.1374mg was used.

A sample of a pharmaceutical was found to exhibit an unusual recrystallisation behaviour over a period of time. This behaviour is often associated with the loss of a solvent from the sample. A method was required to confirm the suspected identity of the solvent which had been used in the production of the sample.

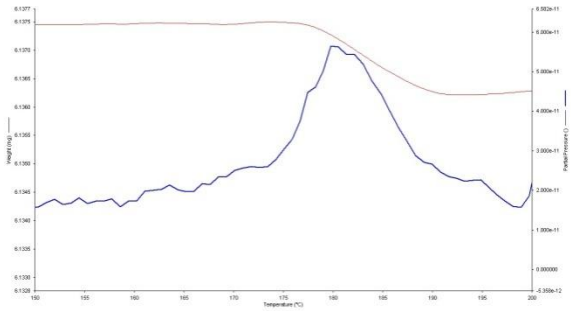
6.1374 mg of the sample was run in the TGA, the HPR-20 mass spectrometer was

used in MID (Multiple Ion Detect) mode using the high sensitivity SEM (Secondary Electron Multiplier) detector. The mass ion chosen to identify the presence of the solvent was 49 amu for Dichloromethane. The following thermogram in the following figure shows the TGA trace collected for the sample. The thermogram shows a very small weight loss of 1.2µg (0.026%).



Weight loss due to the loss of solvent from the sample

This very small weight loss shows the outstanding performance of the Pyris 1 TGA.
The gases evolved during this very small amount of weight loss were analysed and the MS proved that this weight loss was due to loss of dichloromethane from the sample. This is shown in the figure below.



Weight loss and mass 49 (Dichloromethane) trace compared

The analysis of this weight loss is only possible with the unique design of the HPR-20. The use of a wide bore capillary allowing the study of 16 cc/min means that all of the gases from the sample are passed to the mass spectrometer and coupled with the SEM detector; this showed the system is capable of making measurements on weight losses of this small size.

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